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GAGCTCGGAT CCACTACTCG ACCCACCGGT CCGGCCAGGA CCTCTGTGAA CCCGGTGGGG 60
CGGGGGCCGC CTGGCCGGGA GTCTGCTCGG CGGTGGGTGG CCGAGGAAGG GAGAGAACGA 120
TCGGCGGAGCA GGGCGCCCGA ACTCCGGGGCG CCGCGGCC ATG CGC CGG GCC AGC CGA 175
Met Arg Arg Ala Ser Arg
1 5
GAC TAC GGC AAG TAC CTG CGC AGC TCG GAG GAG ATG GGC AGC GGC CCC 223
Asp Tyr Gly Lys Tyr Leu Arg Ser Ser Glu Glu Met Gly Ser Gly Pro
10 15 20
GGC GTC CCA CAC GAG GGT CCG CTG CAC CCC GCG CCT TCT GCA CCG GCT 271
Gly Val Pro His Glu Gly Pro Leu His Pro Ala Pro Ser Ala Pro Ala
25 30 35
CCG GCG CCG CCA CCC GCC TCC CGC TCC ATG TTC CTG GCC CTC CTG 319
Pro Ala Pro Pro Ala Ala Ser Arg Ser Met Phe Leu Ala Leu Leu
40 45 50

FIG. 1A

GGG	CTG	GGA	CTG	GGC	CAG	GTG	GTC	TGC	AGC	ATC	GCT	CTG	TTC	CTG	TAC	367
<u>Gly</u>	<u>Leu</u>	<u>Gly</u>	<u>Leu</u>	<u>Gly</u>	<u>Gln</u>	<u>Val</u>	<u>Val</u>	<u>Cys</u>	<u>Ser</u>	<u>Ile</u>	<u>Ala</u>	<u>Leu</u>	<u>Phe</u>	<u>Leu</u>	<u>Tyr</u>	
55																
TTT	CGA	GCG	CAG	ATG	GAT	CCT	AAC	AGA	ATA	TCA	GAA	GAC	AGC	ACT	CAC	415
Phe	Arg	Ala	Gln	Met	Asp	Pro	Asn	Arg	Ile	Ser	Glu	Asp	Ser	Thr	His	
75																
TGC	TTT	TAT	AGA	ATC	CTG	AGA	CTC	CAT	GAA	AAC	GCA	GGT	TTG	CAG	GAC	463
Cys	Phe	Tyr	Arg	Ile	Leu	Arg	Leu	His	Glu	Asn	Ala	Gly	Leu	Gln	Asp	
90																
TCG	ACT	CTG	GAG	AGT	GAA	GAC	ACA	CTA	CCT	GAC	TCC	TGC	AGG	AGG	ATG	511
Ser	Thr	Leu	Glu	Ser	Glu	Asp	Thr	Leu	Pro	Asp	Ser	Cys	Arg	Arg	Met	
105																
AAA	CAA	GCC	TTT	CAG	GGG	GCC	GTG	CAG	AAG	GAA	CTG	CAA	CAC	ATT	GTG	559
Lys	Gln	Ala	Phe	Gln	Gly	Ala	Val	Gln	Lys	Glu	Leu	Gln	His	Ile	Val	
120																
125																
130																

FIG. 1B

Gly	Pro	Gln	Arg	Phe	Ser	Gly	Ala	Pro	Ala	Met	Met	Glu	Gly	Ser	Trp	135	140	145	150	607
TTG	GAT	GTG	GCC	CAG	CGA	GGC	AAG	CCT	GAG	GCC	CAG	CCA	TTT	GCA	CAC	155	160	165	170	655
Leu	Asp	Val	Ala	Gln	Arg	Gly	Lys	Pro	Glu	Ala	Gln	Pro	Phe	Ala	His	155	160	165	170	175
CTC	ACC	ATC	AAT	GCT	GCC	AGC	ATC	CCA	TCG	GGT	TCC	CAT	AAA	GTC	ACT	170	175	180	185	703
Leu	Thr	Ile	Asn	Ala	Ala	Ser	Ile	Pro	Ser	Gly	Ser	His	Lys	Val	Thr	170	175	180	185	190
CTG	TCC	TCT	TGG	TAC	CAC	GAT	CGA	GGC	TGG	GCC	AAG	ATC	TCT	AAC	ATG	185	190	195	195	751
Leu	Ser	Ser	Trp	Tyr	His	Asp	Arg	Gly	Trp	Ala	Lys	Ile	Ser	<u>Asn</u>	Met					

FIG. 1C

ACG	TTA	AGC	AAC	GGA	AAA	CTA	AGG	GTT	AAC	CAA	GAT	GGC	TTC	TAT	TAC	799
Thr	Leu	Ser	Asn	Gly	Lys	Leu	Arg	Val	Asn	Gln	Asp	Gly	Phe	Tyr	Tyr	
	200					205					210					
CTG	TAC	GCC	AAC	ATT	TGC	TTT	CGG	CAT	GAA	ACA	TCG	GGG	AGC	GTC	847	
Leu	Tyr	Ala	Asn	Ile	Cys	Phe	Arg	His	His	Glu	Thr	Ser	Gly	Ser	Val	
	215				220					225					230	
CCT	ACA	GAC	TAT	CTT	CAG	CTG	ATG	GTG	TAT	GTC	GTT	AAA	ACC	AGC	ATC	895
Pro	Thr	Asp	Tyr	Leu	Gln	Leu	Met	Val	Tyr	Val	Val	Lys	Thr	Ser	Ile	
						235		240			245					
AAA	ATC	CCA	AGT	TCT	CAT	AAC	CTG	ATG	AAA	GGA	GGG	AGC	ACG	AAA	AAC	943
Lys	Ile	Pro	Ser	Ser	His	Asn	Leu	Met	Lys	Gly	Gly	Ser	Thr	Lys	<u>Asn</u>	
						250			255		260					
TGG	TCG	GGC	AAT	TCT	GAA	TTC	CAC	TTT	TAT	TCC	ATA	AAT	GTT	GGG	GGA	991
Trp	Ser	Gly	Asn	Ser	Glu	Phe	His	Phe	Tyr	Ser	Ile	Asn	Val	Gly	Gly	
						265		270			275					

FIG. 1D

FIG. 1

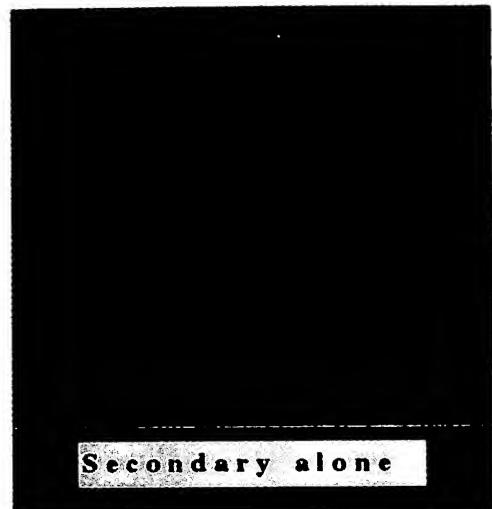
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GTGCCACTGA GAACCTTGA ATTAAAGAGGA TGCCCATGTCA TIGCAAAGAA ATGATAGTGT	1496
GAAGGGTTAA GTTCTTTGAA ATTGTTACAT TGCCTGGGA CCTGCAAATA AGTTCTTTT	1556
TTCTAATGAG GAGGAAAAA TATATGTTATT TTATATATAT GTCTAAAGTT ATATTTCAGG	1616
TGTAATGTT TCTGTGCAA GTTTGTAAA TTATATTGT GCTATAGTAT TTGATTCAA	1676
ATATTTAAA ATGTCCTCACT GTTGACATAT TTAATGTTT AAATGTACAG ATGTATTAA	1736
CTGGTGCCT TTGTATTCC CCTGAAGGTA CTCGTAGCTA AGGGGGCAGA ATACTGTTTC	1796
TGGTGACCACT ATGTTAGTTA TTTCTTTATT CTTTTTAACT TAATAGAGTC TTCAGACTTG	1856

FIG. 1F

TCAAAACTAT GCAAGCAAAA TAAATAAATA AAAATAAAAT GAATACTCTG AATAATAAAGT	1916
AGGATGTTGG TCACCCAGGTG CCTTTCAAAAT TTAGAAGCTA ATTGACTTTA GGAGCTGACA	1976
TAGCCAAAAA GGATACATAA TAGGCTACTG AAATCTGTCA GGAGTATTAA TGCAATTATT	2036
GAACAGGGTGT CTTTTTTTAC AAGAGCTACA AATTGTAAAT TTTGTTCTT TTTTTTCCCA	2096
TAGAAAATGT ACTATAGTT ATCAGCCAAA AAACAATCCA CTTTTTAATT TAGTGAAGT	2156
TATTTTATA TACTGTACAA TAAAAGCATT GTCTCTGAAT GTTAATTTT TGTTACAAAA	2216
AATAAAATTG TACGAAAACC TGAAAAAAA AAAAAAAGGG CGGGCCGCTCT	2276
AGAGGGCCCT ATTCTATAG	2295

FIG. 1G

FIG.2A



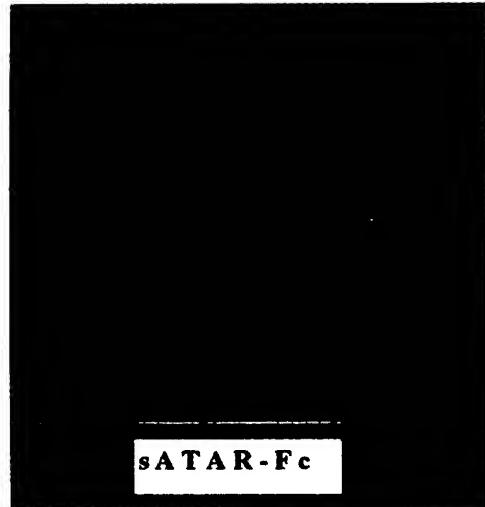
Secondary alone

FIG.2B



OPG-Fc

FIG.2C



sATAR-Fc

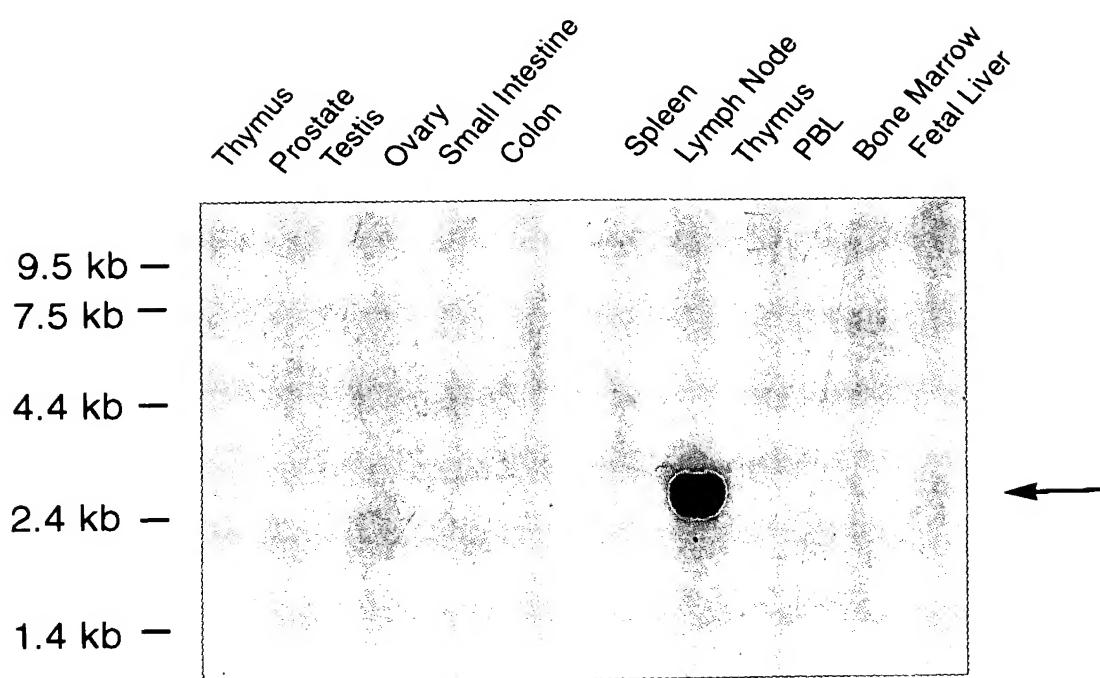


FIG.3

10	30	50						
AAGCTTGGTACCGAGCTCCGATCCACTACTCGACCCACGGCTCCGGCC	AAAGCCGGGCTCCAAAGTCCGGCCCCACGTCGAGGCTCCGCCAGGAGCTCCGGAGCTGGG	CCGAAAGGGAGGGAGGGAGGGAGAGGGAGAGGGAGAGGGAGAGGGAG	CGCCATGCCGCCAGCAGAGACTACACCAAGTACCTGGCTGGCTCGGAGGAGATGGG	GGGGCCCCGGAGCCCCCACGGAGGGCCCCCTGCACGCCGCCCTGCCGCGCA	CCAGCCCCGGCTCCGATGGTCTGGCCCTGGGCTGGGCTGGGCCA	GGTTGCTGCAGCGTCCGGCCCTGGTCTCTATTTCAGAGGGCAGATGGATCCTTAATAGAAT		
70	90	110						
M R R A S R D Y T K Y L R G S E E M G	G G P G A P H E G P L H A P P A P H	M R A S R S M F V A L L G L G L G Q	Q P A A S R S M F V A L L G L G L G Q	Q P A A S R S M F V A L L G L G L G Q	Q P A A S R S M F V A L L G L G L G Q	V V C S V A L F F V F R A Q M D P N R I		
130	150	170						
190	210	230						
250	270	290						
310	330	350						
370	390	410						

FIG. 4A

430 ATCAGAAGATGGCACTCACTGGCATTATAGAATTTCAGACTCCATGAAAATGCAGATT
S E D G T H C I Y R I L R L H E N A D F

450 470

490 TCAAGACACAACTCTGGAGAGTCAGATAACAAATTAAATACCTGATTCTAGGAGAAAT
Q D T T L E S Q D T K L I P D S C R R I

510 530

550 TAAACAGGGCCTTCAAGGGAGCTGTGCAAAAGGAATTACAACATATCGTTGGATCACAGCA
K Q A F Q G A V Q K E L Q H I V G S Q H

570 590

610 CATCAGAGGAGAGAAAGCGATGGATGGCTCATGGCTCATGGTTAGATCTGGCCAAGAGGAGCAA
I R A E K A M V D G S W L D L A K R S K

630 650

670 690 710

730 GCTTGAAGGCTCAGGCCTTTGCTCATCTCACTTAAATGCCACCGACATCCCATCTGGTTC
L E A Q P F A H L T I N A T D I P S G S

750 770

770 CCATAAAAGTGAAGTCTGTCTTGTACCATGATCCGGGTGGCCAAAGATCTCCAAACAT
H K V S L S S W Y H D R G W A K I S N M

FIG. 4B

Title: OSTEOPROTEGERIN BINDING PROTEINS AND RECEPTORS
Inventor: William J. Boyle
Docket No a-451N

790	810	830	
GACTTTAGCAATGGAAACTAATAGTTAATCAGGATGGCTTTATTACCTGTATGCCAA			
T F S N G K L I V N Q D G F Y Y L Y A N			
850	870	890	
CATTGCTTTCGACATCATGAAACTTCAGGAGACCTACAGAGTATCTCAACTAAT			
I C F R H H E T S G D L A T E Y L Q L M			
910	930	950	
GGTGTACGTCACTAAACCAAGCATCAAAATCCCAAGTTCTCATACCCCTGATGAAAGGAGG			
V Y V T K T S I K I P S S H T L M K G G			
970	990	1010	
AAGCACCAAGTATTGGTCAAGGAATTCTGAATCCATTTCATTTCCATAAACGTTGCTGG			
S T K Y W S G N S E F H F Y S I N V G G			
1030	1050	1070	
ATTTTTAAGTTACGGTCTGGAGAGGAAATCAGGCATCGAGGTCTCCAACCCCTCCTTACT			
F F K L R S G E E I S I E V S N P S L L			
1090	1110	1130	
GGATCCGGATCAGGATGCAAACATACTTTGGGGCTTTAAAGTTCGAGATATAGATTGAGC			
D P D Q D A T Y F G A F K V R D I D			

FIG. 4C

1150 CCCAGTTGGAGTGTATGTTACCTGGATGTTGGAAACATTTAAACAGCC
1170
1190
1210 AAGAAAGATGTATAGGTGTTGAGACTAAAGAGGCATGGCCCCAACGGTACACGAC
1230
1250
1270 TCACTATCCATGCTCTGACCTTGTAGAGAACACCCGTATTACAGCCAGTGGAGATGT
1290
1310
1330 TAGACTCATGGTGTGTTACACAATGGTTAAATTGTAAATGAATTCCCTAGAATTAAA
1350
1370
1390 CCAGATTGGAGCAATTACGGGTTGACTTATGAGAAACTGCATGTGGCTATGGGAGGG
1410
1430

FIG. 4D

1450 1470 1490
TTGGTCCCTGGTCATGGCCCCCTTCGCAAGCTGAAGTGGAGAGGGTGTCACTCTAGGGCAAT

1510 1530 1550
TGAAAGGATCATCTGAAGGGCAAAATTCTTTGAATTGTTACATCATGGAACCTGTGCAA

1570 1590 1610
AAAATACTTTCTAATGAGGAGAGAAAATAATATGTTTATAATAATCTAAAGTTA

1630 1650 1670
TATTCAGATGTAATGTTTCTTGCAAAAGTATTGAAATTATATTGTGCTATAGTATT

1690 1710 1730
TGATTCAAAATAATTAAAAATGTCCTGCTGTTGACATATTAAATGTTAAATGTACAGA

1750 1770 1790
CATATTAACTGGTGCACTTGTAAATTCCCTGGGGAAACCTGGCAGGCTAAGGAGGGAA

1810 1830 1850
AAAAATGTTGTTCCCTAAATAATCAAATGCAGTATTCTCGTTCTTAAAGTTAAATAG

FIG.4E

1870	1890	1910	ATTTTTCAGACTTGTCAAGCCTGTGCCAAAAAATTAAATGGATGCCCTTGAATAAAC
1930	1950	1970	CAGGATGTTGCCACCAGGTGCCCTTCAATTAGAAACTAATTGACTTTAGAAAGCTGA
1990	2010	2030	CATTGCCAAAAGGATAACATAATTGGGCCACTGAAATCTGTCAAGAGTAGTTATAATTG
2050	2070	2090	TTGAACACGGTGTTTCCACAAAGTGCCAAATTGTACCTTTTCAAAATAAG
2110	2130	2150	AAAAGTTATTAGTGGTTATCAGCAAAAGTCCAATTAAATTAGTAAATGTTATCTT
2170	2190	2210	ATACTGTACAATAAAACATTGCCCTTGAATGTTAATTGGTACAAAATAAATTAA
2230	2250	2270	TATGAAAAAAAGGGGGCCGCTAGAGGGCCCTATTCTATAG

FIG. 4F

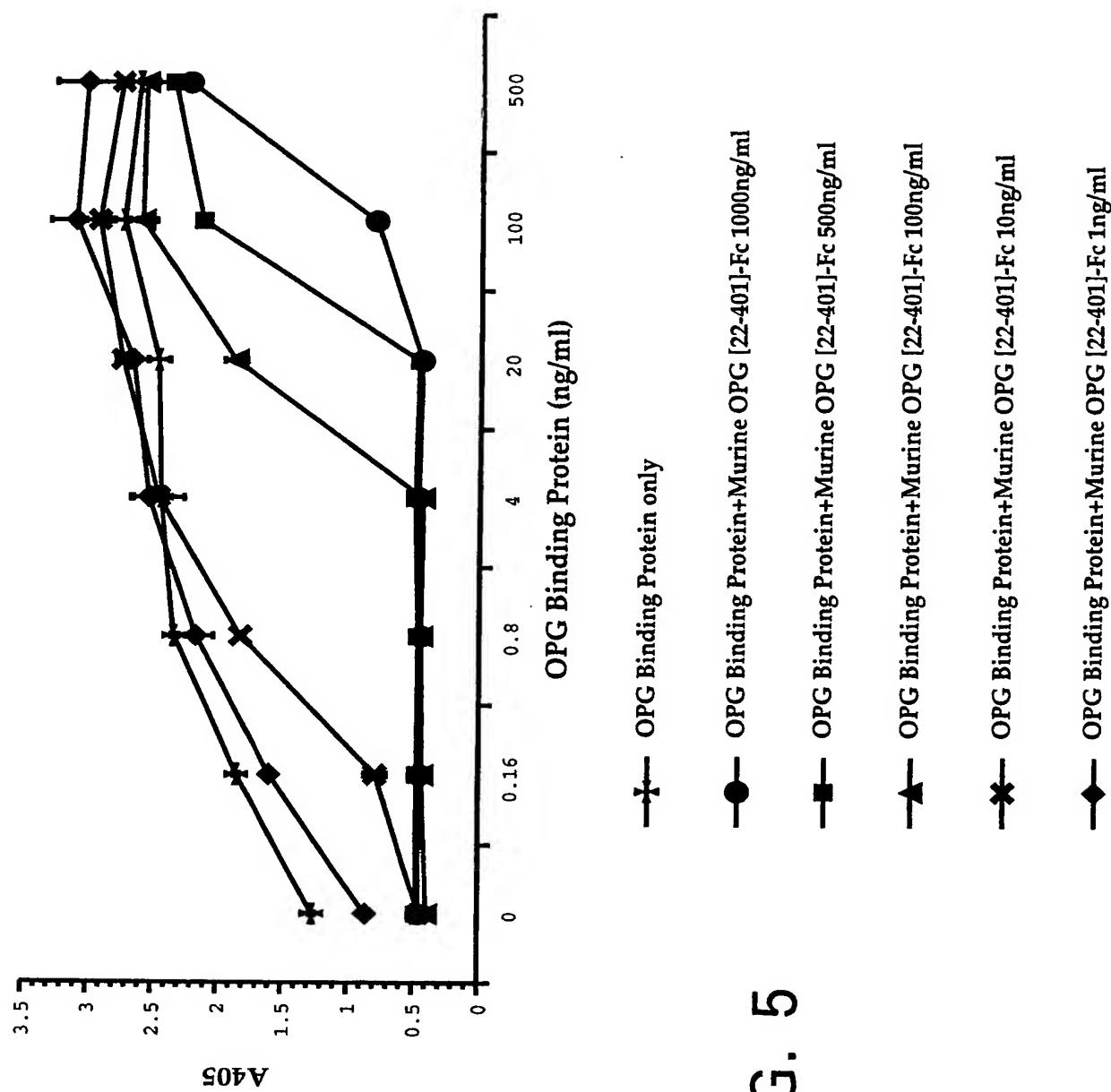


FIG. 5

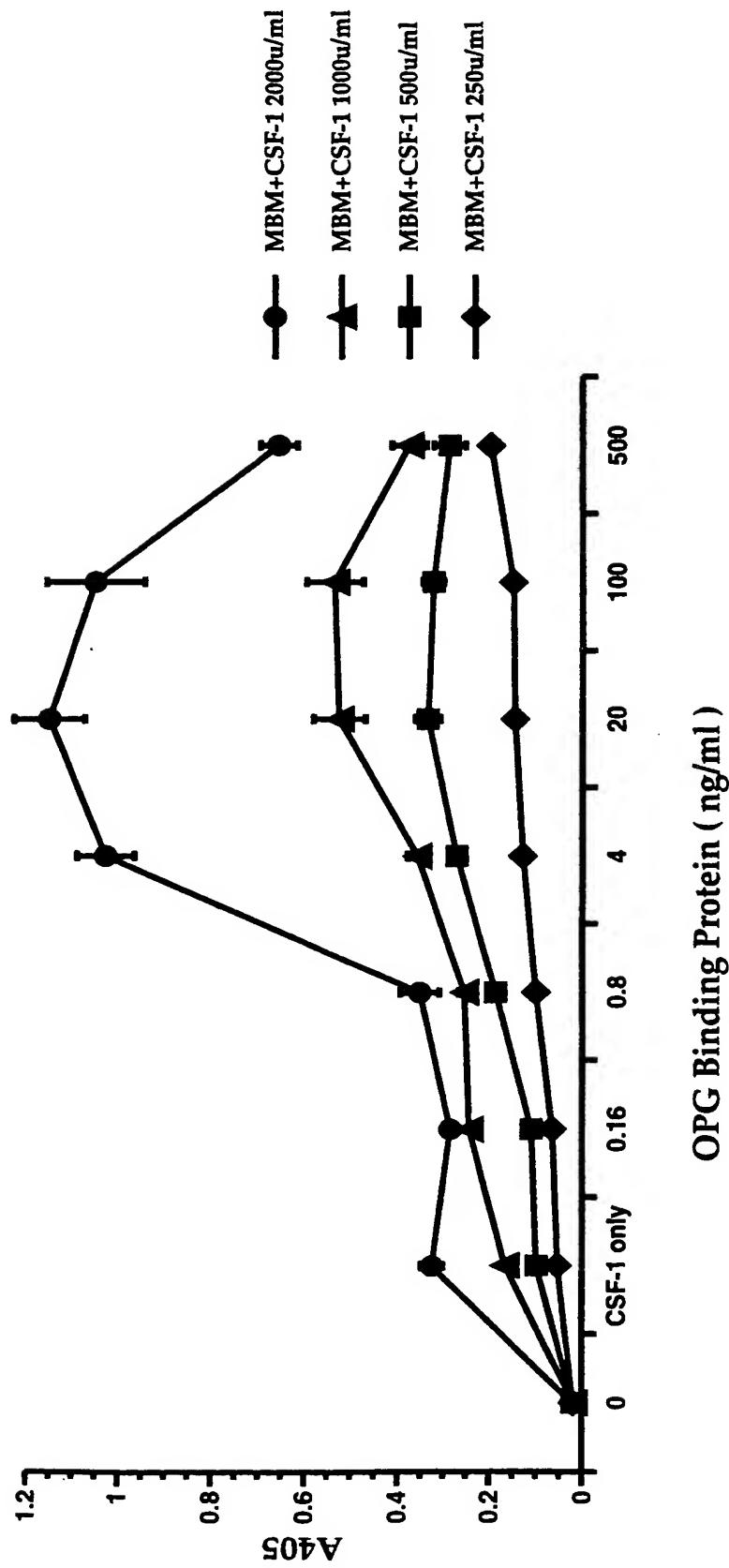


FIG. 6

FIG. 7A

Toluidine Blue Staining



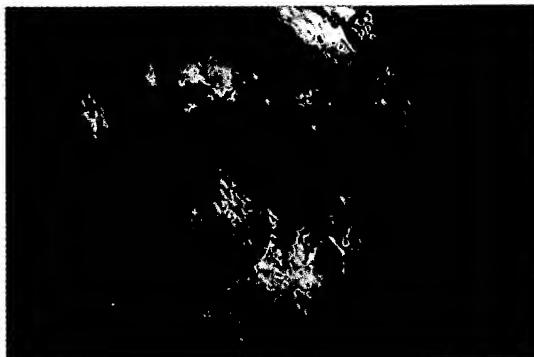
TRAP staining



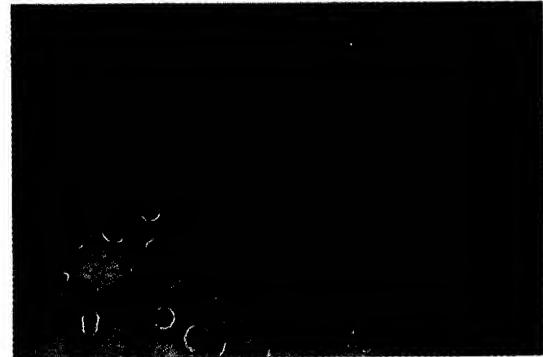
Bone Marrow Cells + M-CSF-1

FIG. 7B

Toluidine Blue Staining



TRAP staining



Bone Marrow Cells + OPG Binding Protein

FIG. 7C

Toluidine Blue Staining



TRAP staining



Bone Marrow Cells + M-CSF-1 +OPG Binding Protein

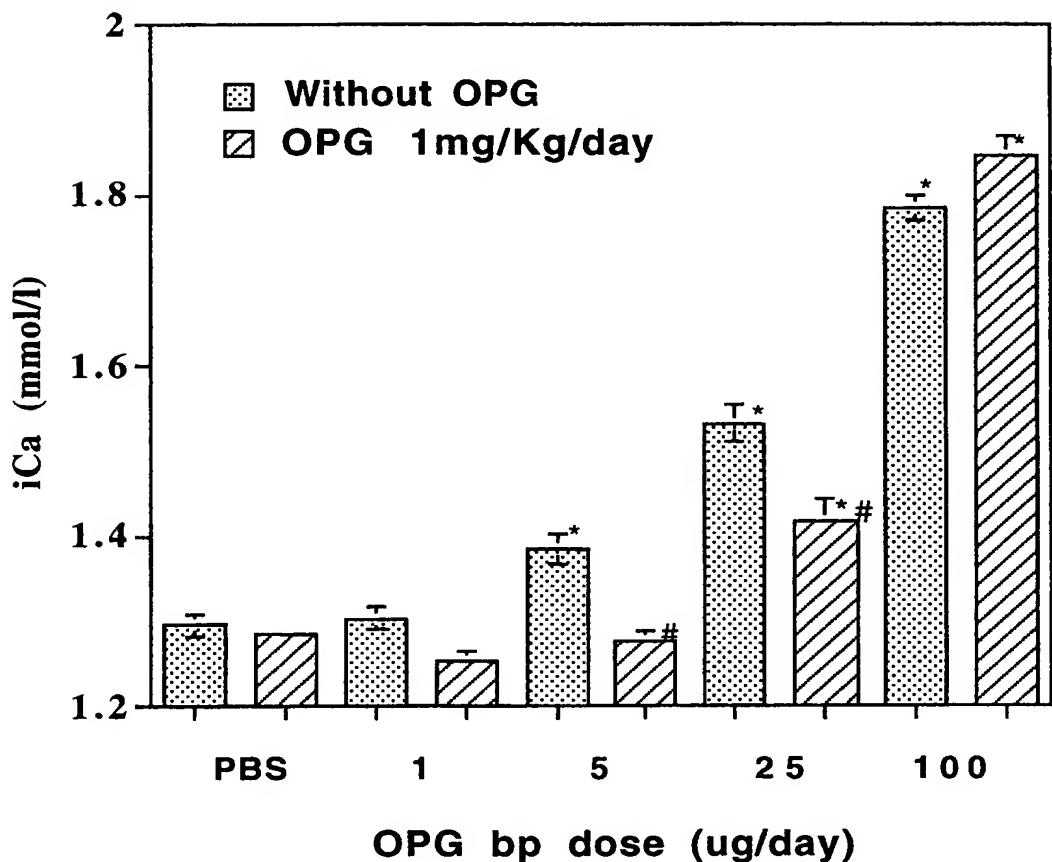
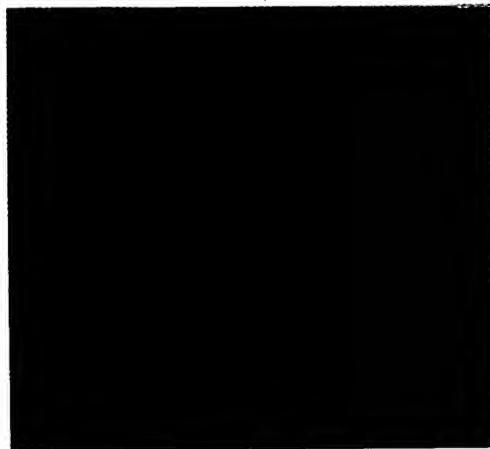


FIG. 8

PBS



OPGbp 5ug/d

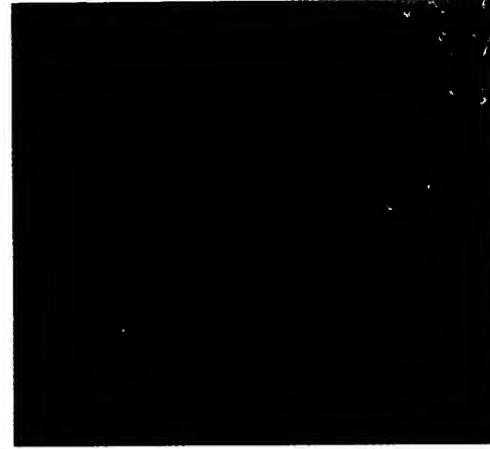
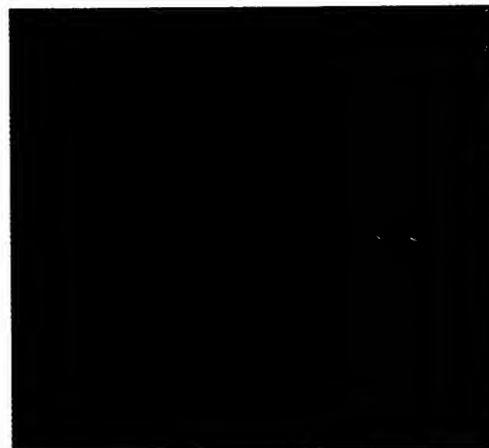


FIG.9A

FIG.9B

OPGbp 25ug/d



OPGbp100ug/d

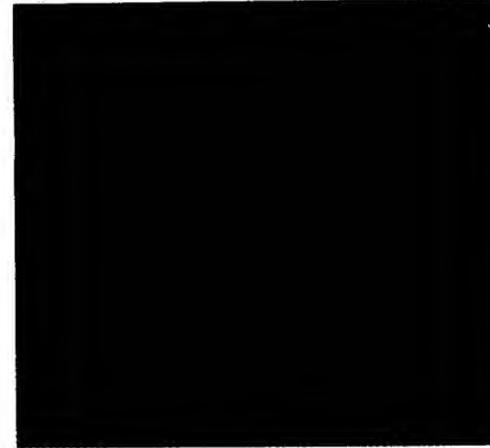


FIG.9C

FIG.9D

FIG. 10A

370	390	410
CCCCGGTCTGCTTGCACGGCTGGCTACCACTGGAACTCAGACTGGAGTCAGCTGGCTGCC		
P R C A C T A G Y H W N S D C E C C R		
430	450	470
GCAGGAAACACGGAGTGTGCACCTGGCTTCGGAGCTCAGCATTCCCTTGCAGCTCAACAAAGG		
R N T E C A P G F G A Q H P L Q L N K D		
490	510	530
ATACGGTGTGCACACCCCTGCCCTGGCTTCTCAGATGTCAGATGTCAGATGTCAGATGTCAGACA		
T V C T P C L L G F F S D V F S S T D K		
550	570	590
AATGCAAACCTTGGACCAACTGCACCCCTTGGAAAGCTAGAAGCACACCAGGGGACAA		
C K P W T N C T L L G K L E A H Q G T T		
610	630	650
CGGAATCAGATGTTGGTCTGCAGACACTGACCATGAGGAGACCCAAAGGAGGCC		
E S D V V C S S S M T L R R P P K E A Q		

FIG. 10B

670	690	710
A Y L P S L I V L L F I S V V V V A A		
730	750	770
CCATCATCTTCCGGCTTACTACAGGAACGGAGGGAAAGCGCTGACAGCTAATTGTGGA		
I I F G V Y Y R K G G K A L T A N L W N		
790	810	830
ATTGGGTCAATGATGCTTGCAGTAGTCTAAAGTGAATAAGGAGTCCTCAGGGGACCGTT		
W V N D A C S S L S G N K E S S G D R C		
850	870	890
GTGCTGGTTCCCACTCGGCAACCTCCAGTCAGCAAGAAGTGTGTGAAGGTATCTTACTAA		
A G S H S A T S S Q Q E V C E G I L L M		
910	930	950
TGACTCGGGAGGAGAAGATGGTTCAGAAGACGGTGTGGAGTCTGTGGCCTGTGTGTG		
T R E E K M V P E D G A G V C G P V C A		
970	990	1010
CGGCAGGTTGGGCCCTGGGAGAAGTCAGAGATTCTAGGACGCTCACACTGGTCAAGCGAGG		
A G G P W A E V R D S R T F T L V S E V		

FIG. 10C

FIG. 10D

1390 1410 1430
AGGACCATGAAACCCTTCCAGGGTCCCTGAAATGTGGACCATTGCCAGTGTGCCTACA
D H E P F P G S L K C G P L P Q C A Y S
1450 1470 1490
GCATGGCTTCCAGTGAAGCAGCAGGCCAGCATGGCAGAGGGGGAGTACGGCCCCAGG
M G F P S E A A S M A E A G V R P Q D
1510 1530 1550
ACAGGGCTGATGAGGGAGCCTCAGGGTCCGGAGGCTCCCCCAGTGACGCCACCTG
R A D E R G A S G S G S P S D Q P P A
1570 1590 1610
CCTCTGGAACGTGACTGGAAACAGTAACCTCACGTTCATCTCTAGGGCAGGTGATGA
S G N V T G N S N S T F I S S G Q V M N
1630 1650 1670
ACTTCAAGGGTGCACATCATCGTGGTGTATGTCAAGCCAGACCTCGCAGGAGGGGGGT
F K G D I I V V Y V S Q T S Q E G P G S
1690 1710 1730
CCGCAGAGCCGAGTCCGGAGCCGCTGTGCAGGGAGACGCCACACA
A E P E S E P V G R P V Q E E T L A H R

FIG. 1OE

1750	1770	1790
GAGACTCCTTGTGGGCACCGCGCTTCCCCGACGTCTGTGCCACCGGGCTGGGC		
D S F A G T A P R F P D V C A T G A G L		
1810	1830	1850
TGCAGGAGCAGGGGCACCCCGGCAGAACGGACGGGACATCGGGGGTGCAGGAGGG		
Q E Q G A P R Q K D G T S R P V Q E Q G		
1870	1890	1910
GTGGGGCGCAGACTTCACTCCATACCCAGGGTCCGGACAATGTGCAGAACATGACCTCACC		
G A Q T S L H T Q G S G Q C A E		
1930	1950	1970
TTCTCTGTCTGCCCTGGGTGCAGGGCACCAAGTGCCTTCCAAAAACATGGTGTAGCTAGC		
1990	2010	2030
CACTGTGCACCTCCCTCACTGGCAGGGCTGCTGGCATGGGAGCCACCTCTCACT		
2050	2070	
TCCTCCAGTGGCCCTCTCCCTCTGCCTCTCCCTAC		

FIG. 10F



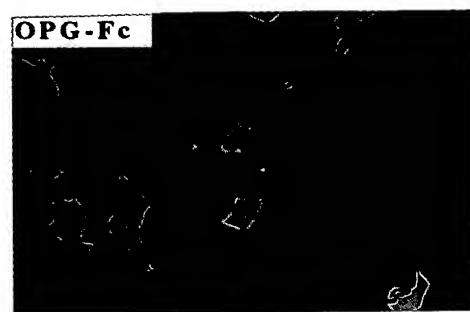
FIG.11A



FIG.11B



FIG.11C



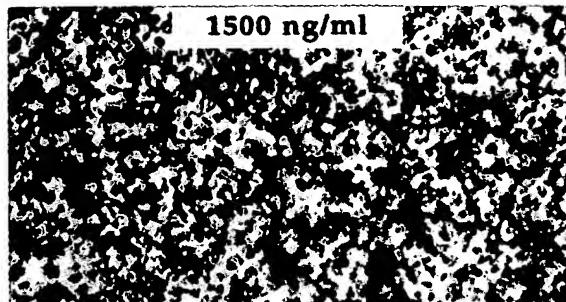


FIG.12A

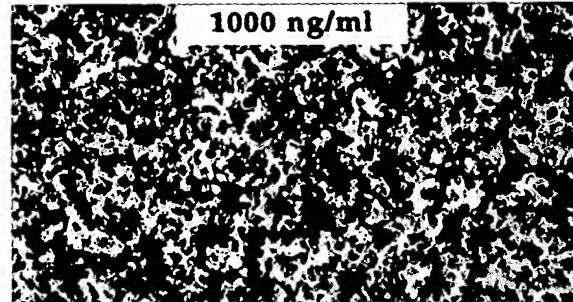


FIG.12B

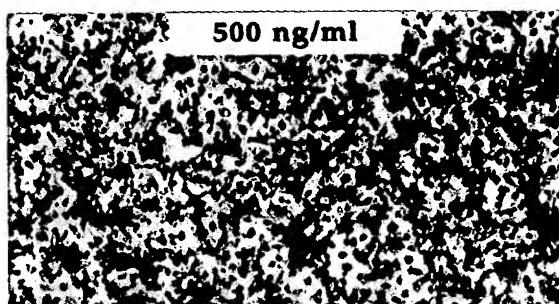


FIG.12C

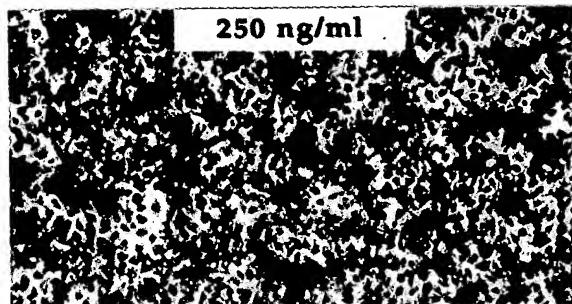


FIG.12D

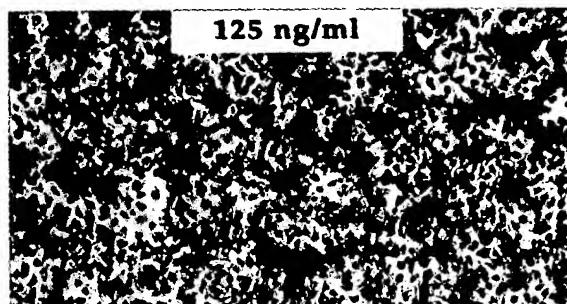


FIG.12E

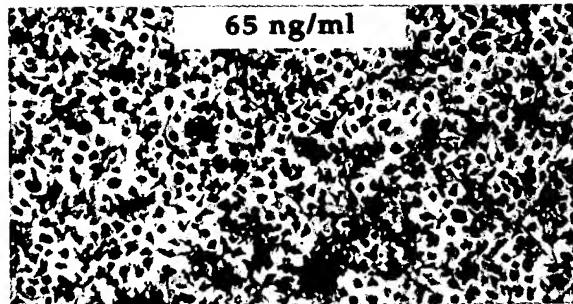


FIG.12F

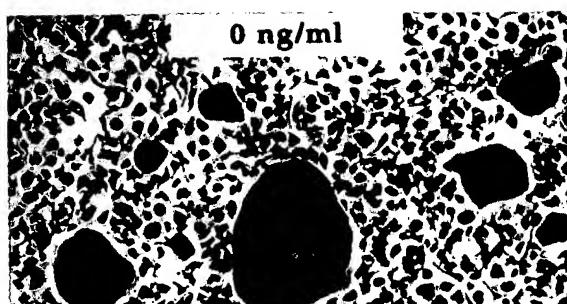
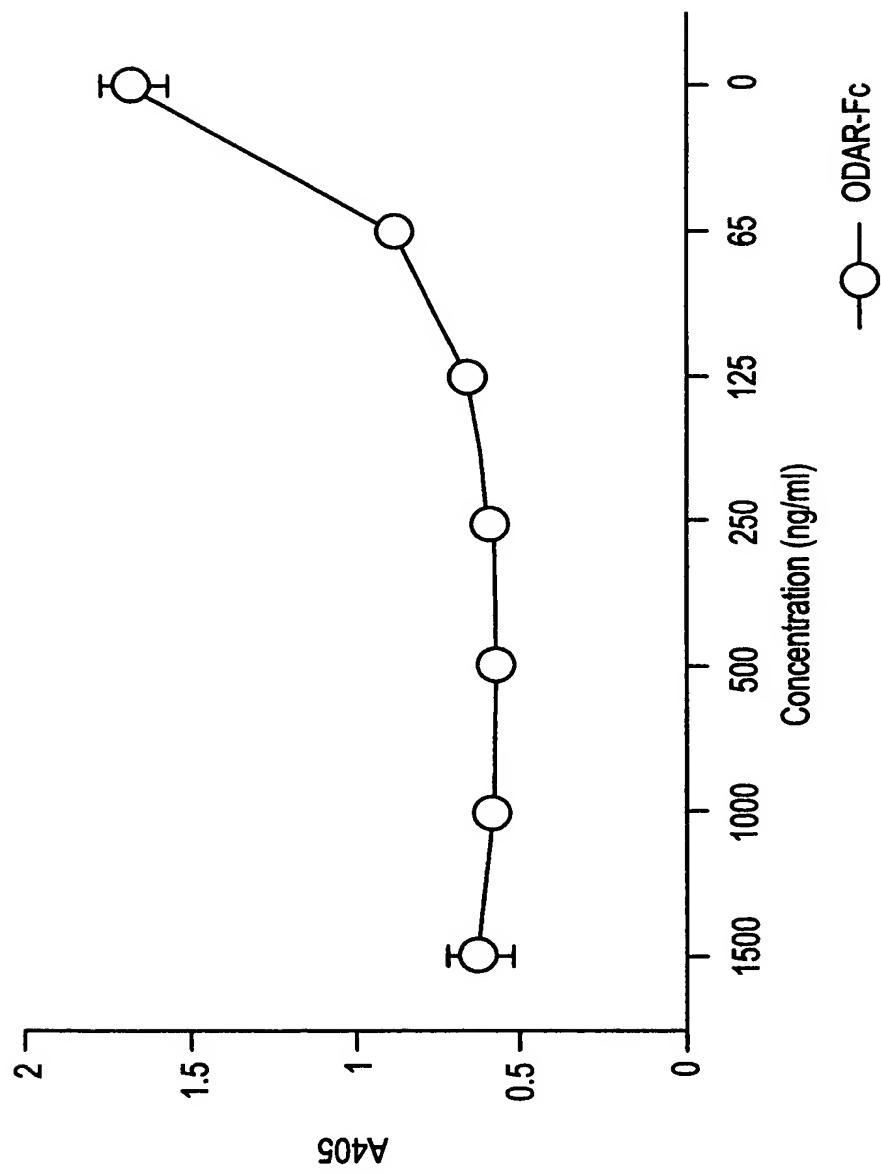
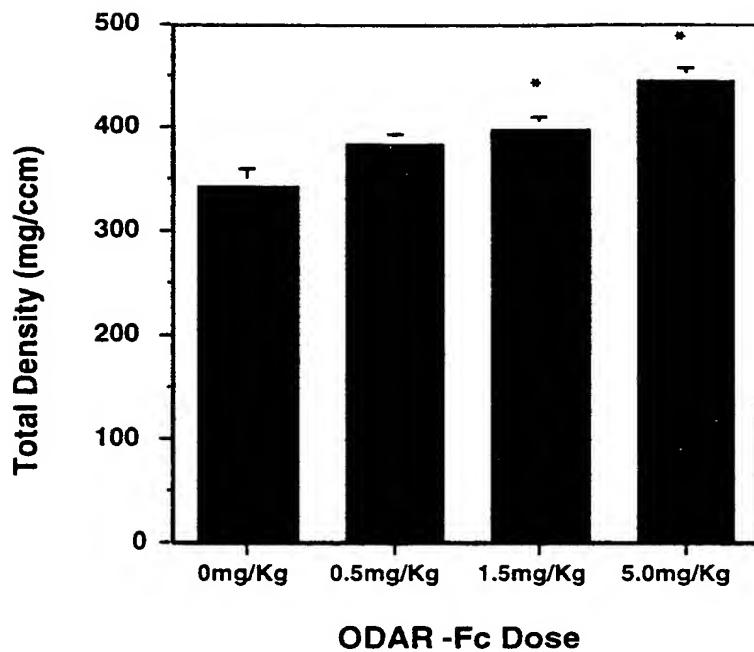


FIG.12G

FIG. 12H





* Different to vehicle treated control $p < 0.05$.

FIG. 13